fragment of the present invention has been clarified. Claim 15 has been cancelled without prejudice and incorporated into claim 14. New claim 25 has been added. Support for claim 25 is found throughout the specification, e.g., at page 21, lines 9-14. Thus no new matter has been added. The above amendments have been made to more fully protect the invention disclosed and to particularly set forth and distinctly claim the present invention.

In light of the above amendments and following discussions, applicants respectfully request that the outstanding rejections be withdrawn and the claims be allowed.

A petition for an extension of time of three (3) months for responding to the outstanding Office Action and the appropriate fee is enclosed herewith.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

The Examiner has requested that the Applicant transfer the CRF containing the Sequence Listing from either parent Application into the present Application. Applicant respectfully submits that such a request was filed with the divisional application. Applicants have included a copy of the request to this Amendment.

Claims 14-19 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

The present invention relates to a method for preventing or treating Sjögren's syndrome which comprises administering to a patient a therapeutically effective amount of α-fodrin, a mutein thereof, an antigenic fragment thereof, or a salt thereof with a pharmaceutically acceptable carrier. The present inventors were the first to

discover that α-fodrin or a fragment thereof is an autoantigen specific to Sjögren syndrome (SS) patients and the first to confirm that the suppression of the autoantigen can lead to the suppression the symptom of Sjögren's syndrome. The present invention provides a method of prophylaxis and treatment of Sjögren's syndrome, based on the finding that the α-fodrin and a fragment thereof are the autoantigens of Sjögren syndrome.

In the field of immunology, one of ordinary skill in the art would recognize that when an autoantigen of certain immunological disease is identified, the administration of that autoantigen to a human patient can induce immunotolerance against not only B cells but also T cells, even though the route and method of administration needs to be modified. Applicants have included herewith an excerpt from the textbook entitled "IMMUNOLOGY", which is a basic text in the field of immunology. Applicants refer the Examiner to page 171, where it states that "Very large doses of antigen often result in specific T-and sometimes B-cell tolerance." (see Attachment 1, page 171, paragraph of "Large doses of antigen can induce tolerance"). Thus, one of ordinary skill in the art would recognize that identification and administration of an autoantigen can easily lead to "immunotolerance".

Thus, Applicants respectfully submit that there is sufficient description of the present invention.

It is the to the Examiner's position that the use of protein as a therapeutic agent is unpredictable. Contrary to this position, Applicants respectfully submit that a number of various proteins (e.g., tPA, growth hormone) have been commercialized for use as pharmaceuticals. Thus, one of ordinary skill in the art would not consider that the use of protein as a pharmaceutical agent is unpredictable.

The Examiner cites Tisch et al. as teaching that administration of an antigen peptide to treat an ongoing T-cell-mediated autoimmunity may exacerbate the disease condition. Applicants respectfully disagree. It is known that an antigen can induce immune response or immunotolerance depending on the administration route. (See "IMMUNOLOGY", page 172). Thus, the Examiner's application of the teachings of Tisch et al., to the present invention is not appropriate.

In addition, Applicants submit herewith experimental data supplied by the inventors. (Attachment 2). This data shows that the α-fodrin and a fragment thereof of the present invention are usable as a therapeutic agent for "already established Sjögren disease patients". The test animal, Sjögren's Syndrome Model NFS/sld Mouse, used for this experiment developed SS in 4-20 weeks from thymus removal on day 3 after birth, as described in Experiment 1 in the specification. In the Experiment in Attachment 2, administration of the α-fodrin fragment protein 4-7 weeks later resulted in the suppressive effect on the symptoms of SS. These results demonstrate that α-fodrin fragment protein of the present invention has a therapeutic effect after the onset of SS.

The Examiner also states that "besides the specific polypeptide fragment of α-fodrin disclosed in the specification, the specification fails to provide any guidance as to how to determine the active amino acid residues within the scope of the claimed invention". Applicants respectfully disagree with the Examiner's position.

At the time the application was filed, an "immunochemically equivalent" fragment could be obtained easily by those of ordinary skill in the art, if the moiety showing the antigen specificity could be specified. The specification teaches that a method using protease, recombinant biotechnology, and a method using chemical synthesis (pages 7-20) can be used to obtain an "immunochemically equivalent" fragment.

When determining the activity, since Sjögren's Syndrome Model NFS/sld Mouse described in the present specification was known when the application was filed (see Example 1 in the specification), whether or not the obtained fragment is an "immunochemically equivalent fragment" could be confirmed easily using this model.

Thus, the specification provides sufficient information for one of ordinary skill in the to practice the invention.

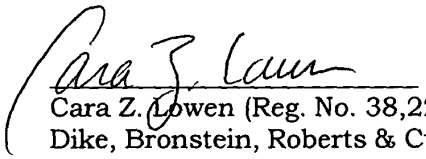
Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

Claim 17 stands rejected under 35 U.S.C. 112, second paragraph, because it has an amino acid sequence but no SEQ ID NO. The above amendment to claim 17 obviates this rejection.

In view of the above discussion and amendment, it is respectfully submitted that the present application is in condition for allowance. Therefore, an early reconsideration and allowance are respectfully requested.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

Respectfully submitted,



Date: July 25, 2001

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"VERSION WITH MARKINGS TO SHOW CHANGES MADE."

IN THE SPECIFICATION:

On page 1, line 8, please insert the following:

--This application is a divisional of 09/076,938, which issued as U.S. Patent No. 6,121,057 on September 19, 2000, which is divisional of 08/736,434.--

IN THE CLAIMS

Please amend the claims as follows:

14. (amended) A method for preventing or treating ~~autoimmune disease~~ Sjögren's syndrome which comprises administering to a patient a therapeutically effective amount of α-fodrin, a mutein thereof, an antigenic fragment thereof, or a salt thereof with a pharmaceutically acceptable carrier.

Please cancel claim 15, without prejudice.

16. (amended) The method of claim ~~15~~ 14, wherein the molecular weight of said α-fodrin, a mutein thereof, or an antigenic fragment thereof is from about 2K to about 240K.

17. (amended) The method of claim ~~15~~ 14, wherein said α-fodrin, a mutein thereof, or an antigenic fragment thereof contains or comprises an amino acid sequence substantially shown by Arg-Gln-Lys-Leu-Glu-Asp-Ser-Tyr-Arg-Phe-Gln-Phe-Phe-Gln-Arg-Asp-Ala-Glu-Glu-Leu (SEQ ID NO:1).

18. (amended) The method of claim 17, wherein the molecular weight of said α-fodrin, a mutein thereof, or an antigenic fragment thereof is from about 100K to about 140K.

Please add the following claim:

--25. The method of claim 14, wherein Sjögren's syndrome is a symptom of inflammations of lacrimal or salivary glands.--